Patent
Attorney's Docket No. 029430-497

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| In re Patent Application of | ) | |
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| Kunihiko MORIZANE et al. | ) | Group Art Unit: Unassigned |
| | ) | |
| Application No.: Unassigned | ) | Examiner: Unassigned |
| | ) | |
| Filed: December 13, 2001 | ) | |
| | ) | |
| For: METHOD FOR PRODUCING CYTIDINE DERIVATIVES | ) | |

**PRELIMINARY AMENDMENT**

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

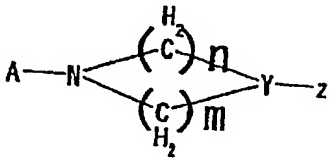
Prior to the first Official Action, please amend the above-identified patent application as follows:

**IN THE CLAIMS:**

Kindly amend claims 4-10 and 13 as follows:

4. (Amended) The method for producing cytidine derivatives according to Claim 1, where said tertiary amine is an alicyclic amine represented by formula (4):

(4)



wherein, n and m each independently represent an integer of 1 to 4, Y represents hydrogen atom, carbon atom, nitrogen atom, oxygen atom, sulfur atom, Z represents hydrogen atom, an alkyl group having 1 to 4 carbon atoms, an alkyl group having 1 to 4 carbon atoms substituted with a halogen atom(s), an alkenyl group having 2 to 4 carbon atoms, or Z attached to A may form a ring, A represents an alkyl group having 1 to 4 carbon atoms, an alkyl group having 1 to 4 carbon atoms substituted with a halogen atom(s), an alkenyl group having 2 to 4 carbon atoms, or A attached to Z may form a ring.

6. (Amended) The method for producing cytidine derivatives according to Claim 1, where said tertiary amine is an aliphatic amine represented by formula (6):

(6) 


wherein, R6, R7 and R8 each independently represent an alkyl group having 1 to 4 carbon atoms, a cycloalkyl group having 5 to 8 carbon atoms, an alkyl group having 1 to 4 carbon atoms substituted with a halogen atom(s), or an alkenyl group having 2 to 4 carbon atoms.

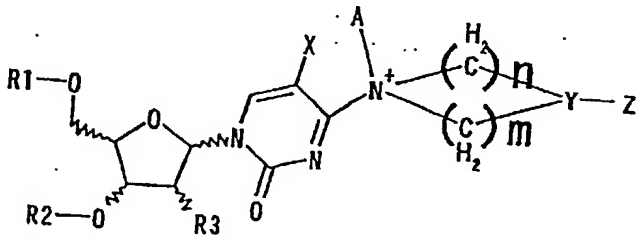
7. (Amended) The method for producing cytidine derivatives according to Claim 1, wherein said tertiary amine is N-methylpiperidine, N-methylmorpholine, 1,4-diazabicyclo[2.2.2]octane, N,N'-dimethylpiperazine, or trimethylamine.

8. (Amended) The method for producing cytidine derivatives according to Claim 1, characterized in that said dehydrating reactant is acid halides or acid anhydrides, and said reaction is carried out in the presence of a deacidifying agent.

9. (Amended) The method for producing cytidine derivatives according to Claim 8, wherein said deacidifying agent is p-toluenesulfonyl chloride.

10. (Amended)The method for producing cytidine derivatives according to Claim 1, wherein the molar ratio of said tertiary amine to said uridine derivative represented by formula (1) is 1.2 or less.

11. (Amended)A cytidine derivative represented by formula (5):

(5) 

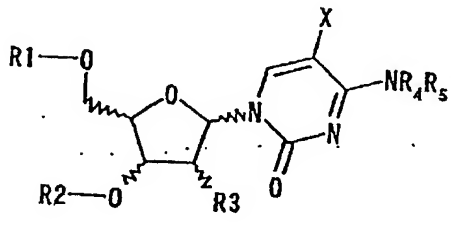

wherein, X represents a hydrogen atom, a halogen atom, an alkyl group having 1 to 4 carbon atoms, an alkyl group having 1 to 4 carbon atoms substituted with a halogen atom(s), or an alkenyl group having 2 to 4 carbon atoms, R1 and R2 each independently represent either a hydrogen atom or a hydroxyl-protecting group, R3 represents a hydrogen atom, a halogen atom, a hydroxyl group, an alkyl group having 1 to 4 carbon atoms, a

cyano group, an alkenyl group, an alkynyl group, an alkoxy group having 1 to 4 carbon atoms, a hydroxyl group substituted with a hydroxyl-protecting group, n and m each independently represent an integer of 1 to 4, Y represents hydrogen atom, carbon atom, nitrogen atom, oxygen atom, sulfur atom, Z represents hydrogen atom, an alkyl group having 1 to 4 carbon atoms, an alkyl group having 1 to 4 carbon atoms substituted with a halogen atom(s), an alkenyl group having 2 to 4 carbon atoms, or Z attached to A may form a ring, A represents an alkyl group having 1 to 4 carbon atoms, an alkyl group having 1 to 4 carbon atoms substituted with a halogen atom(s), an alkenyl group having 2 to 4 carbon atoms, or A attached to Z may form a ring, or salts thereof.

13. (Amended)A method for producing a cytidine derivative represented by formula (3):

(3)

(3)




wherein, X represents a hydrogen atom, a halogen atom, an alkyl group having 1 to 4 carbon atoms, an alkyl group having 1 to 4 carbon atoms substituted with a halogen atom(s), or an alkenyl group having 2 to 4 carbon atoms, R1 and R2 each independently represent either a hydrogen atom or a hydroxyl-protecting group, and R3 represents a hydrogen atom, a halogen atom, a hydroxyl group, an alkyl group having 1 to 4 carbon

atoms, a cyano group, an alkenyl group, an alkynyl group, an alkoxy group having 1 to 4 carbon atoms, a hydroxyl group substituted with a hydroxyl-protecting group, and R4 and R5 each independently represent a hydrogen atom, an alkyl group having 1 to 4 carbon atoms, a cycloalkyl group having 5 to 8 carbon atoms, an alkyl group having 1 to 4 carbon atoms substituted with a halogen atom(s), or an alkenyl group having 2 to 4 carbon atoms, or R4 and R5 linked together may form a ring, characterized in that the cytidine derivative or salts thereof according to Claim 11 is reacted with ammonia or a primary or secondary amine.

## REMARKS

By the present Preliminary Amendment, all multiple dependency has been eliminated from the original claims so that the amended claims encompass certain aspects of the invention within the original multiple dependent claims. It is to be understood that the revisions to the claims are solely for formalistic purposes and not with regard to patentability and that applicants reserve the right to pursue claims directed to other aspects of the invention encompassed by the original multiple dependent claims or described in the specification. In addition, independent claims 11 and 13 have been amended to provide the definitions of the groups referred to in previous claims. It is to be understood that these revisions in claims 11 and 13 does not alter the scope thereof.

Entry of the instant Preliminary Amendment and favorable consideration on the merits are respectfully requested.

Should the Examiner have any questions concerning the subject application, the Examiner is invited to contact the undersigned attorney at the number provided below.

Respectfully submitted,

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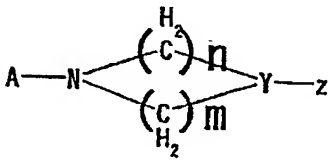
Date: December 13, 2001

**Attachment to Preliminary Amendment dated December 13, 2001**

**Marked-up Claims 4, 6-11 and 13**

4. (Amended) The method for producing cytidine derivatives according to Claim 1 [to 3], where said tertiary amine is an alicyclic amine represented by formula (4):

(4) 

wherein, n and m each independently represent an integer of 1 to 4, Y represents hydrogen atom, carbon atom, nitrogen atom, oxygen atom, sulfur atom, Z represents hydrogen atom, an alkyl group having 1 to 4 carbon atoms, an alkyl group having 1 to 4 carbon atoms substituted with a halogen atom(s), an alkenyl group having 2 to 4 carbon atoms, or Z attached to A may form a ring, A represents an alkyl group having 1 to 4 carbon atoms, an alkyl group having 1 to 4 carbon atoms substituted with a halogen atom(s), an alkenyl group having 2 to 4 carbon atoms, or A attached to Z may form a ring.

6. (Amended) The method for producing cytidine derivatives according to Claim 1 [to 3], where said tertiary amine is an aliphatic amine represented by formula (6):

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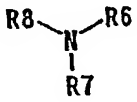
**Marked-up Claims 4, 6-11 and 13**

(6)




wherein, R6, R7 and R8 each independently represent an alkyl group having 1 to 4 carbon atoms, a cycloalkyl group having 5 to 8 carbon atoms, an alkyl group having 1 to 4 carbon atoms substituted with a halogen atom(s), or an alkenyl group having 2 to 4 carbon atoms.

7. (Amended) The method for producing cytidine derivatives according to Claim 1 [to 6], wherein said tertiary amine is N-methylpiperidine, N-methylmorpholine, 1,4-diazabicyclo[2.2.2]octane, N,N'-dimethylpiperazine, or trimethylamine.

8. (Amended) The method for producing cytidine derivatives according to Claim 1 [to 7], characterized in that said dehydrating reactant is acid halides or acid anhydrides, and said reaction is carried out in the presence of a deacidifying agent.

9. (Amended) The method for producing cytidine derivatives according to Claim [1 to] 8, wherein said deacidifying agent is p-toluenesulfonyl chloride.

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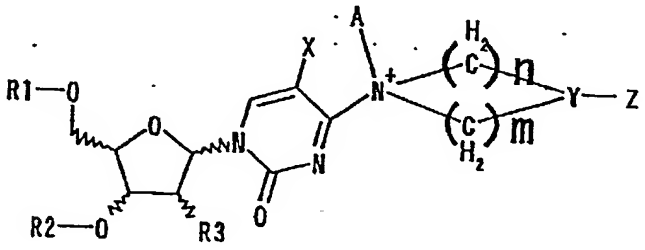
**Marked-up Claims 4, 6-11 and 13**

10. (Amended)The method for producing cytidine derivatives according to Claim 1 [to 9], wherein the molar ratio of said tertiary amine to said uridine derivative represented by formula (1) is 1.2 or less.

11. (Amended)A cytidine derivative represented by formula (5):

(5) 

wherein, [X, R1, R2, R3, n, m, A, Y and Z are as defined above,] X represents a hydrogen atom, a halogen atom, an alkyl group having 1 to 4 carbon atoms, an alkyl group having 1 to 4 carbon atoms substituted with a halogen atom(s), or an alkenyl group having 2 to 4 carbon atoms, R1 and R2 each independently represent either a hydrogen atom or a hydroxyl-protecting group, R3 represents a hydrogen atom, a halogen atom, a hydroxyl group, an alkyl group having 1 to 4 carbon atoms, a cyano group, an alkenyl group, an alkynyl group, an alkoxy group having 1 to 4 carbon atoms, a hydroxyl group substituted with a hydroxyl-protecting group, n and m each independently represent an integer of 1 to 4, Y represents hydrogen atom, carbon atom, nitrogen atom, oxygen atom, sulfur atom, Z represents hydrogen atom, an alkyl group having 1 to 4 carbon atoms, an alkyl group

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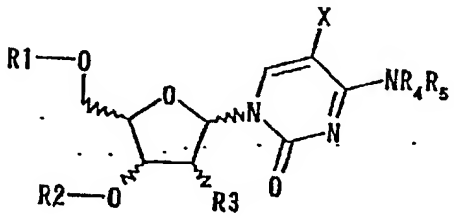
**Marked-up Claims 4, 6-11 and 13**

having 1 to 4 carbon atoms substituted with a halogen atom(s), an alkenyl group having 2 to 4 carbon atoms, or Z attached to A may form a ring, A represents an alkyl group having 1 to 4 carbon atoms, an alkyl group having 1 to 4 carbon atoms substituted with a halogen atom(s), an alkenyl group having 2 to 4 carbon atoms, or A attached to Z may form a ring, or salts thereof.

13. (Amended)A method for producing a cytidine derivative represented by formula (3):

(3) 


wherein, [X, R1, R2, R3, R4 and R5 are as defined above] X represents a hydrogen atom, a halogen atom, an alkyl group having 1 to 4 carbon atoms, an alkyl group having 1 to 4 carbon atoms substituted with a halogen atom(s), or an alkenyl group having 2 to 4 carbon atoms, R1 and R2 each independently represent either a hydrogen atom or a hydroxyl-protecting group, and R3 represents a hydrogen atom, a halogen atom, a hydroxyl group, an alkyl group having 1 to 4 carbon atoms, a cyano group, an alkenyl group, an alkynyl group, an alkoxy group having 1 to 4 carbon atoms, a hydroxyl group

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**Marked-up Claims 4, 6-11 and 13**

substituted with a hydroxyl-protecting group, and R4 and R5 each independently represent a hydrogen atom, an alkyl group having 1 to 4 carbon atoms, a cycloalkyl group having 5 to 8 carbon atoms, an alkyl group having 1 to 4 carbon atoms substituted with a halogen atom(s), or an alkenyl group having 2 to 4 carbon atoms, or R4 and R5 linked together may form a ring, characterized in that the cytidine derivative or salts thereof according to Claim 11 [and 12] is reacted with ammonia or a primary or secondary amine.